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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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03/27/2002 7116 03/27/2002 PIRULI, PIRULI, JR.

B 1645

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EXAMINER

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1645

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No. 08/702,718

Applicant(s)

Muller-Rober et al.

Examiner

Phuong Bui

Group Art Unit

1645



Responsive to communication(s) filed on Oct 12, 1999

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 1-14, 16-24, 28-39, 41, and 43-73 is/are pending in the application.

Of the above, claim(s) 4, 6-14, 16, 19, 22, 23, 29-38, 41, 44-48, 50, 51, 53, 55, 57, 60, 63-65, 67, 68 is/are withdrawn from consideration.

Claim(s) 17 and 71 is/are allowed.

Claim(s) 1-3, 5, 18, 20, 21, 24, 28, 39, 43, 49, 52, 56-58, 61, 62, 66, 69, 70, 72, ⁷³ is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of restriction election, Amendment E, Paper No. 19, filed October 12, 1999. Applicant elects Group I and species VI, with traverse. Applicant primarily traverses that (1) the transgenic plant of Group I should not be separated from the storage organ of Group III because a storage organ of a transgenic plant is part of the transgenic plant, and a search for a transgenic plant having reduced citrate synthase activity would necessarily be coextensive with a search for the storage organ of the plant; (2) the process claims of Groups III and IV should not be separated from the process claims of Group I because the process claims of all three groups are directed to a process of reducing citrate synthase activity in transgenic plant cells, and thus a search of the process claims of Group I would necessarily be coextensive with a search of the process claims of Groups III and IV; (3) the claims of Groups I, III and IV are classified in the same class and subclass (class 800, subclass 205) and therefore a search of the prior art for Group I would be coextensive with a search of Groups III and IV and there would be no serious burden for the Examiner to search these groups together (Applicant noted that the International Preliminary Examination Authority acknowledged unity of invention under PCT Rule 13); and (4) each of species with the exception of Species XI encodes citrate synthase and thus together they define a single general inventive concept, and a search for a transgenic plant comprising a construct encoding citrate synthase in the antisense orientation would encompass all species of citrate synthase.

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Applicant's traversal is unpersuasive for the following reasons:

While Applicant asserts that the search for one invention would be coextensive with the search of another, these assertions are unsupported on the record. The position of the Office is that, while the searches may be expected to overlap, there is no reason to believe that the searches would be coextensive. Specifically, regarding inventions I and III, the focus of invention I is to inhibit flower formation, whereas the focus of invention III is to improve storage capability. This contrast is clearly laid out in claims 21 and 22. Although a storage organ may be part of a transgenic plant, Applicant has not demonstrated that, in searching the transgenic plant of invention I for plants having inhibited flower formation, the entire search for storage organs having improved storage capability would be performed. In addition, Applicant has not contested the patentable distinctiveness of these inventions. Applicant should note that searches in technologies such as that of the instant case rely heavily on automated commercial databases which are terminology specific. There is no reason to expect that a database search for invention I would of necessity require searching for storage organs. Moreover, though each of inventions I, III and IV require reduced citrate synthase activity, the desired outcomes of such reduced activity for each invention is divergent. The database searches would require searching for these differences. Thus, the searches would not in fact be coextensive. Even though the U.S. Patent Classifications are the same, these divergent database searches represent a significant burden to the Office. Finally, Applicant has not established that a search for one of the delineated species would encompass a search of all the species. The database search for one species would be

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expected to be specific for that species only. If evidence is uncovered during the search for the elected species which would render one or more of the non-elected species unpatentable, then the species election with regard to those species will be withdrawn.

Accordingly, claims 1-14, 16-24, 28-39, 41 and 43-73 are pending. Claims 4, 6-14, 16, 19, 22, 23, 29-38, 41, 44-48, 50, 51, 53-55, 59, 60, 63-65, 67, and 68 are nonelected. Claims 1-3, 5, 17, 18, 20, 21, 24, 28, 39, 43, 49, 52, 56-58, 61, 62, 66 and 69-73 to the extent of species VI (citrate synthase of *S. tuberosum* or SEQ ID NO:1) are examined in the instant application.

Information Disclosure Statement

2. An initialed copy of Applicant's form 1449 (Paper No. 8) is attached to this Office action.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

4. The abstract of the disclosure is objected to because it is not written in a single paragraph format. Correction is required. See MPEP § 608.01(b).

35 U.S.C. 112, second paragraph

5. Claims 1-3, 5, 18, 20, 21, 24, 28, 39, 43, 49, 52, 56-58, 61, 62, 66 and 69, 70, 72 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 1 and all claims which recite “reduced” or “reducing”, “reduced” is a relative term lacking a comparative basis. Also, in claim 1, it is unclear what the plant is displaying when it is “displaying inhibition of flower formation”. Does Applicant mean that the plant does not flower?

In claims 2, 3 and 24, it is unclear what is doing the “inhibiting”.

In claim 5, “useful” is a relative term lacking a comparative basis.

In claim 18, it is unclear whether or not “(DSM 8880)” is synonymous with plasmid pKS-CSa, the abbreviation for pKS-CSa, or is the deposit accession number for said plasmid.

Claim 20 is an improper multiple dependent claim (MPEP 608.01(n)). Furthermore, it is unclear whether Applicant intends to claim a bacterial cell or the vector. Also, claim 20 depends from nonelected claim 19. Claim 20 and all other claims which depend from nonelected claims must be amended accordingly in response to this Office action. For future reference, it is suggested that dependent claims should follow, rather than precede, the claim(s) which they depend from.

Claim 24 is a method claim which lacks positive steps.

In claim 28, it is unclear by “said DNA sequence” whether Applicant is referring to the “recombinant DNA” in (a) or the “DNA sequence” recited in (ii) of claim 73. Also, the metes and bounds of “essentially identical”, “a part of” and “part thereof” are unclear. All other recitations of “essentially identical” in other claims are also unclear. Furthermore, “derived by insertion, deletion or substitution from the nucleotide sequence of SEQ ID NO:” is unclear because it is unclear which region of said SEQ ID NO. is retained in the resulting derivative, and it is unclear

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whether the recited SEQ ID NO. is utilized for inserting/deleting/substituting into an undisclosed sequence, or whether undisclosed insertion/deletion/substitution is made into the recited SEQ ID NO. Further, “a high degree of homology” and “sufficient” are a relative terms lacking a comparative basis. It is also unclear how “an antisense effect” is defined. Further, the last word of claim 28, “gene”, should be “genes” for proper antecedence.

Claim 39 lacks positive steps.

In claim 43, it is unclear by “originates” how far back in evolution Applicant intends to go. Which part of the original DNA is retained in the claimed DNA molecule?

Amended claim 49 should be clarified as “(twice amended)” since it was already amended in the preliminary amendment of October 16, 1997.

Claim 56 is an improper multiple dependent claim. Further, it is unclear whether Applicant intends to claim a bacterial cell, a plasmid comprising the DNA molecule (what DNA molecule?), or the plasmid of any one of claims 53-55 (which are nonelected claims).

In claim 58, it is unclear what protein is expressed from “expressing from said DNA molecule non-translatable RNA”. Expression is understood by one skilled in the art to mean protein expression. However, if the RNA is non-translatable, then it is unclear what protein is expressed.

In claim 61, the EC number should follow “citrate synthase”, not “family”.

In claim 73(ii), “expressed” should be amended to “transcribed” since “expressed” is understood by one skilled in the art to be related to protein expression.

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Clarification and/or correction are required.

35 U.S.C. 112, first paragraph

6. Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is invited to point to the page and line number in the specification for "non-translatable RNA". Amending "mRNA" to "RNA" broadens the scope of the claim. Absent of such support, Applicant is required to cancel the new matter in response to this Office action.

7. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is unclear that the claimed plasmid pKS-CSa (DSM 8880) is readily available to the public or easily reproducible by one skilled in the art. If not, a deposit of said plasmid necessary to practice the claimed invention and in compliance with 37 C.F.R. 1.801-1.809 will be required. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably

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removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R.

1.808. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Absent of further guidance, one skilled in the art cannot practice the claimed invention without undue experimentation.

8. Claims 1-3, 5, 18, 20, 21, 24, 28, 39, 43, 49, 52, 56-58, 61, 62, 66 and 69, 70, 72 and 73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antisense RNA of SEQ ID NO:1 or of the nucleotide sequence encoding citrate synthase, does not reasonably provide enablement for any method of inhibiting flower formation by reducing citrate synthase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. With the exception of the use of the antisense sequence of SEQ ID NO:1, Applicant does not teach other methods for reducing citrate synthase activity resulting in inhibition of flower formation. Claim 1 in particular reads on transgenic plants with reduced citrate synthase due to undisclosed mechanisms, i.e., there is no relationship between the plant being transgenic and its having reduced citrate synthase activity. However, the state of the prior art is that citrate synthase is involved in multiple pathways not fully understood by those skilled in the art. Other than by the use of the antisense sequence, it is unpredictable to determine what mechanism(s) or compounds would inhibit or reduce citrate synthase activity or expression of endogenous DNA sequences which encode citrate synthase, as cited in claim 2. In reference to claim 3, it is unclear how one skilled in the art would be able to determine what

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antisense RNA other than the antisense RNA of the citrate synthase gene would inhibit endogenous citrate synthase expression without further guidance and undue experimentation. Furthermore, what level of citrate synthase activity would inhibit flower formation? Landschuetze et al. (EMBO Journal, 14(4), 1995, p. 660-666 Applicant's Information Disclosure Statement) teaches, using the antisense RNA approach, in the resulting transgenic potato plants with a strong reduction in citrate synthase activity (less than 30% of wild-type levels), flower buds formed at least two weeks later as compared with wild-type plants (Abstract). While these flower buds were aborted at an early stage of development, there is flower formation nevertheless. Therefore, again, other than the use of the antisense RNA, Applicant provided no guidance as to what other method would reduce citrate synthase by at least 30% resulting in inhibition of flower maturation (not flower formation). In reference to claim 28, it is an invitation to experiment requiring undue experimentation for one skilled in the art to determine which part of SEQ ID NO:1 (part can be as little as 1 nucleotide) or which insertion/deletion/substitution of SEQ ID NO:1 would "elicit an antisense effect" without further guidance as to how inoperable embodiments can be predictably and reliably eliminated without undue experimentation. In claim 39, again, other than the antisense molecule of the gene encoding citrate synthase, Applicant does not teach how a DNA molecule which codes for citrate synthase should be used to inhibit flower formation, which Applicant has not shown. In claim 58, there is no evidence that the synthesis of endogenous citrate synthase is prevented, that plants do not require citrate synthase, and that the "non-translatable RNA" is able to block all synthesis of endogenous citrate synthase. In fact,

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Landschuetze et al. would indicate to the contrary (Table I). In claim 61, a coding region could be as little as one codon, which is unlikely to work based upon the state of the prior art and Applicant's lack of evidence to the contrary. Furthermore, even if it is the full coding region of the gene encoding citrate synthase, it is unclear how such a coding region, operably linked to a promoter, transcribed to mRNA to result in expression of more citrate synthase, would suppress the activity of endogenous citrate synthase and inhibit flower formation, especially when Applicant's disclosure indicated otherwise (specification, p. 3, ln. 2-5). The scope of the claim encompasses a promoter operably linked to the full coding sequence for citrate synthase, yet Applicant does not teach that an increased level of citrate synthase in the cell would suppress the activity of endogenous citrate synthase. In claim 72, again, other than the antisense RNA to the gene encoding citrate synthase, Applicant does not teach any other antisense RNA which inhibit expression of endogenous citrate synthase genes. In claim 73, a DNA sequence complementary to the citrate synthase gene reads on a 2-nucleotide sequence, which is unlikely to work based upon the state of the prior art and Applicant's lack of evidence to the contrary. Accordingly, without further guidance to the above issues, one skilled in the art cannot make and use the invention as commensurate in scope with the claims without undue experimentation.

Remarks

9. Claims 17 and 71 are allowable. SEQ ID NO:1 is free of the prior art. The prior art fails to provide motivation for generating a recombinant dsDNA molecule comprising a promoter and a DNA sequence coding for a citrate synthase, wherein the DNA sequence is fused to the

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promoter in antisense orientation so that the non-coding strand of the DNA sequence is transcribed.

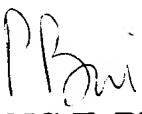
10. Papers relating to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1648, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Bui whose telephone number is (703) 305-1996. The Examiner can normally be reached Monday-Friday from 6:30 AM - 4:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Phuong Bui
Patent Examiner
Group Art Unit 1648
December 29, 1999


PHUONG T. BUI
PATENT EXAMINER